Homogeneous Catalysis by Gold

A. Stephen K. Hashmi
Institut für Organische Chemie, Universität Stuttgart, Pfaffenwaldring 55, D-70569 Stuttgart, Germany
http://www.hashmi.de

A comprehensive overview in the field of homogeneous catalysis by gold is given and the basic principles are discussed. It is also highlighted where homogeneous gold catalysts are already superior to other catalysts and where future possibilities for advantageous use of homogeneous gold catalysts exist.

For a long time, gold was considered to possess only low catalytic activity ("catalytically dead") and therefore only its stoichiometric co-ordination and organo-metallic chemistry was investigated intensively. Even in the 19th century it was quite popular to characterize precious alkaloid bases after their troublesome isolation from natural sources as tetrachloroaurates (1,2).

Since then, a change of paradigm has taken place (3). Among the numerous applications for gold, its use as a catalyst, albeit not yet consuming large amounts of this metal, has attracted much attention. Overall, in the chemical databases ca. 230,000 papers on gold can be found, of which about 9,000 deal with gold catalysis (from the SciFinder database in October 2003). The field of gold catalysis is dominated by heterogeneous catalysts, while homogeneous catalysts still represent the much smaller part (about 100 hits). Still, a significant amount of different homogeneous gold-catalysed reactions is known and basic principles can be deduced from them.

In this article only publications in which gold is unambiguously the site of the catalysis reaction will be covered. This, for example, excludes the use of some mixed metal clusters and mixed metal colloids.

Background

Homogeneous catalysis includes all reactions in which the substrate(s) and the catalyst are in the same state. As there exists only a limited number of highly volatile gold compounds, most of these reactions are conducted in the liquid phase with either liquid or dissolved substrate(s) and a dissolved catalyst. Homogeneous catalysis in the solid state, a part of the solvent-free reactions (4) that are nowadays quite popular in the field of green chemistry, has not been explored with gold yet (with the exception shown in Figure 31)! In this context, the non-toxicity of gold, which helps to avoid any environmental problems, is also of importance.

The catalyst itself promotes a chemical reaction, a process in which chemical compounds (the substrates) are converted to other chemical compounds (the products), to proceed under milder reaction conditions (lower temperatures, lower pressure, lower concentrations of the substrates, higher or different selectivity). As the catalyst is not consumed, a catalytic amount is sufficient – but this is often a matter of debate: for some scientists 20 mol% of 'catalyst' are still catalytic, while others may consider this to be a sub-stoichiometric reaction and accept only 0.001 mol% or less as catalytic.

Two motives drive the desire to produce a chemical reaction:

1 A chemical compound is unwanted (for example

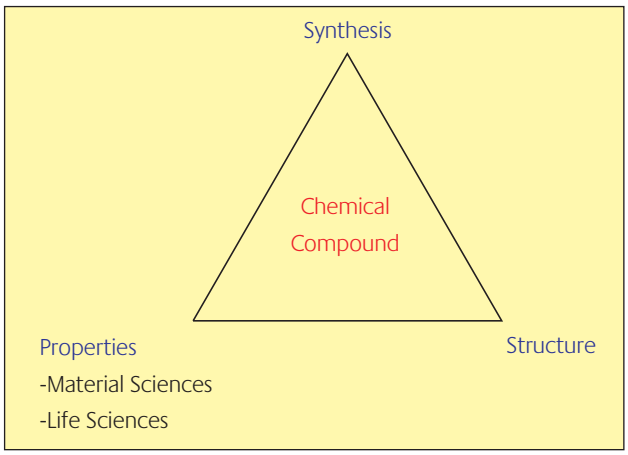

Figure 1
The three important features of chemical compounds

poisonous) and is converted to environmentally acceptable compounds (waste management).

2 A desired chemical compound is produced that way (synthesis of bulk or fine chemicals). With chemical compounds always three things are associated: their synthesis, their structure and their properties. The need for chemical compounds stems from their properties in either the field of materials science or life science.

As always in life, costs are crucial.

The use of gold as a catalyst is desirable when it has a similar activity as for a more expensive catalyst, when it shows a higher activity or a higher selectivity than less expensive catalysts and when a completely new chemical transformation is possible using the gold catalyst.

In the past century the number of publications on gold catalysis per year has increased exponentially (Figure 2). While the absolute numbers are not debatable, one should ask what this really means. In every conference similar graphs are presented and one learns that the number of publications in that specific field shows exponential growth. How can that be, every field is getting more important? The explanation is simple, the number of scientific publications itself resembles an exponential growth. So the exponential growth of the sheer number of publications on gold catalysis itself might only mean that the field is keeping pace with all the other fields (for all publications in the field of chemistry, see Figure 3). Whether the field is able to claim a higher percentage of all chemical publications and thus has truly gained in significance can be determined by normalization. The division of the numbers in Figure 2 by the numbers in Figure 3 gives the numbers in Figure 4. The good news is that indeed gold catalysis has occupied an increasing portion of the chemical literature, since the 80's roughly a 400% increase has taken place!

The following sections are arranged in the sequence in which the reaction principles were first discovered. All later

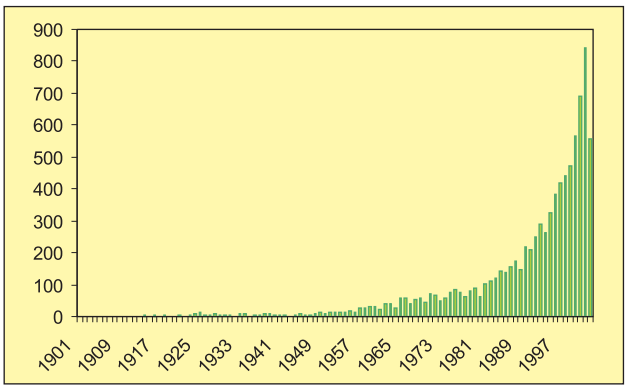

Figure 2
Total number of publications on gold catalysis per year

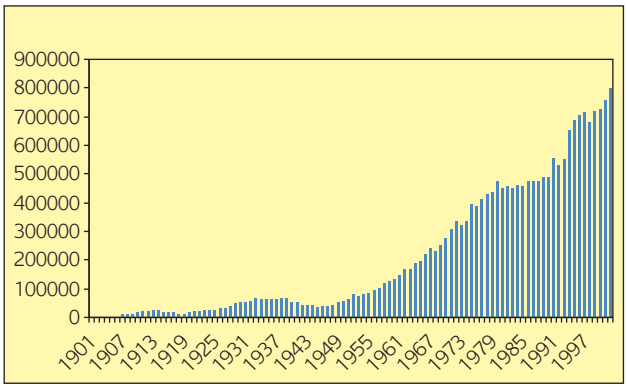

Figure 3
Total number of all chemical publications per year

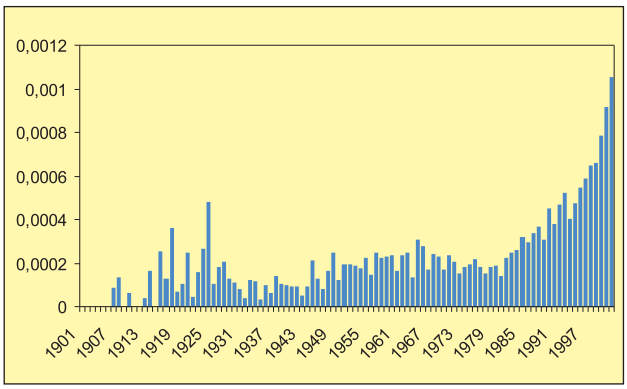

Figure 4
Normalized number (percentage of all chemical publications) of publications on gold catalysis per year

variations or related reactions are then placed in the same section. The turnover numbers (TON) and turnover frequencies (TOF) can be deduced from the amount of catalyst and the yield. The important *new bonds* formed in the catalysis reactions are highlighted in red.

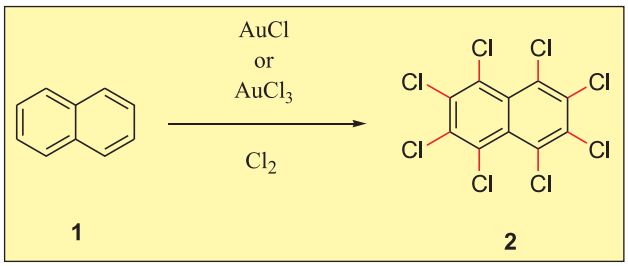

Figure 5
Complete substitution of all hydrogen atoms of napthalene by chlorine

The Beginning

In 1935, it was reported that both AuCl and $AuCl_3$ catalyse the chlorination of naphthalene **1** to octachloronaphthalene **2** (5), Figure 5.

The authors found gold to be among the most active catalysts, but as we know today, other Lewis-acid catalysts such as $FeCl_3$ are superior for these reactions.

Strained Compounds

In 1972, gold was still considered to possess low reactivity, thus the investigation of a highly reactive substrate was quite logical. Several different late transition metals were assessed for the isomerisation of the bicyclo[1.1.0]butane **3**. With AuI_3 at 0°C four products **4-7** were obtained, Figure 6. $PdCl_2$, which is a d^8-system like Au(III), gives an analogous product ratio, while for example $RhCl_3 \cdot H_2O$ produced an entirely different product distribution (6).

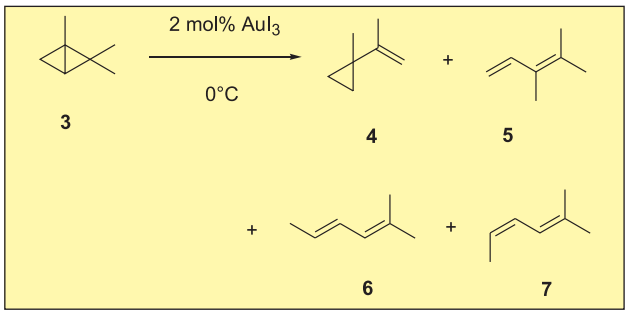

Figure 6
Four different products from the isomerisation of an unsymmetrical bicyclo[1.1.0]butane

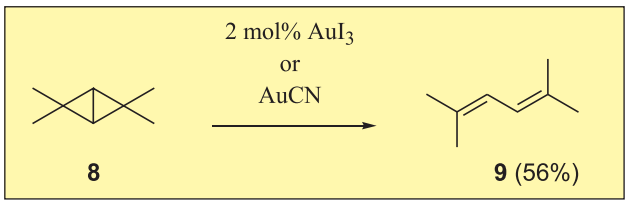

Figure 7
Only one product from the symmetric bicyclo[1.1.0]butane

The symmetric bicyclo[1.1.0]butane **8** provided only one product **9**, Figure 7. Here AuI_3 induced a much faster reaction than AuCN; but the best yield was obtained with $Cu(BF_4)_2 \cdot H_2O$.

In 1976, de Meijere *et al.* wanted to investigate the thermolysis of diamedane **10** to triquinacene **11**. A reactor with a gold surface was built, in the expectation that this surface would be inert. To their surprise they discovered that snoutene **12** was formed, Figure 8. Subsequently, they found that not only the gold surface but also gold complexes e.g. $AuCl(C_{10}H_{12})$ ($C_{10}H_{12}$ = dicyclopentadiene) are capable of catalysing this conversion (7).

Oxidation Reactions

This area of investigation was initiated by Natile *et al.* in 1983. The selective oxidation of thioethers **13** to sulfoxides **14** with gold, known as a stoichiometric reaction since 1905 (8), can be achieved in a catalytic manner using a gold terachloroaurate in the presence of HNO_3 (9,10), Figure 9.

The chemoselectivity of the reaction was high, and the presence of vinyl groups, tertiary amines, alcohols and diols was tolerated. With chiral thioethers a single diastereomer of the product was detected. Subsequently it was discovered that the corresponding tetrabromoaurate was even more active (11).

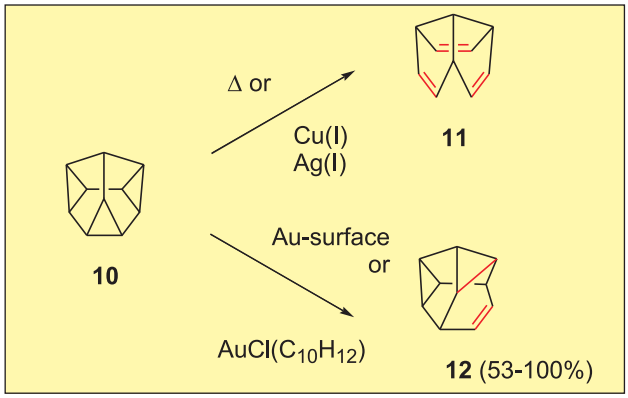

Figure 8
Even the surface of elemental gold was active

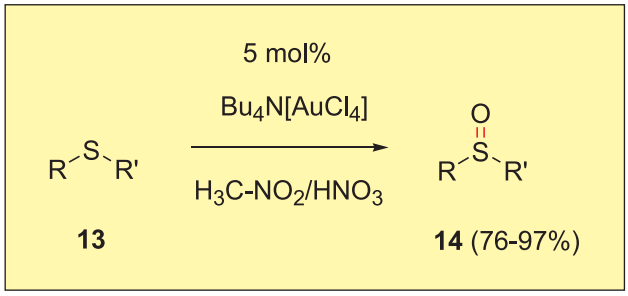

Figure 9
Highly selective oxidation of thioethers

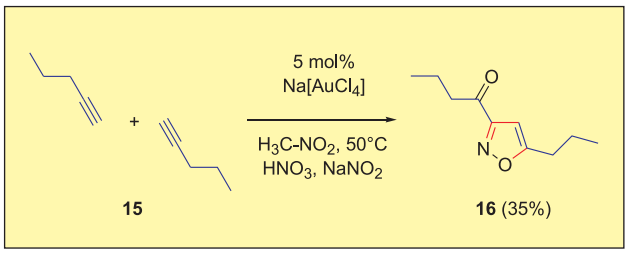

Figure 10
Synthesis of isoxazoles under oxidative conditions

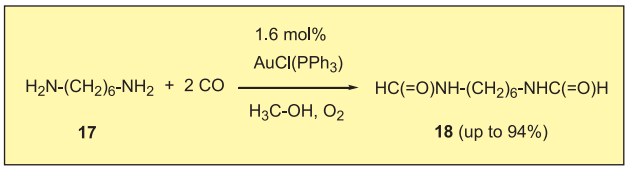

Figure 11
Synthesis of formamides from CO under oxidative conditions

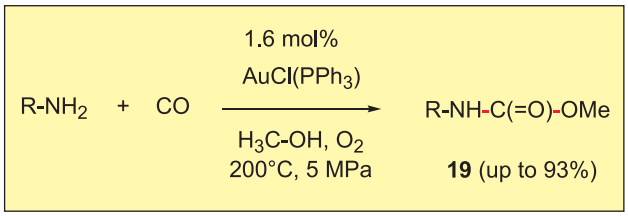

Figure 12
Synthesis of carbamates from CO under more forcing oxidative conditions

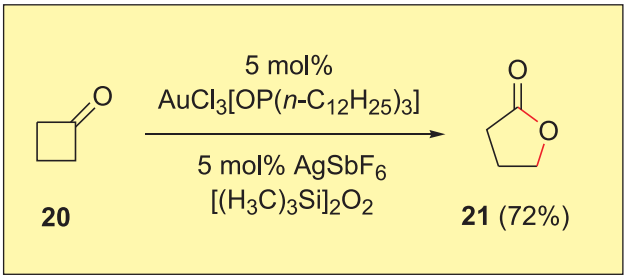

Figure 13
*Baeyer-Villiger oxidation to cyclic lactones **21***

A true breakthrough was finally achieved by Hill *et al.* who used a combinatorial catalyst design and discovered that with $H[AuCl_4]/AgNO_3$ in acetonitrile under 1 atmosphere of oxygen or even air can be used as the oxidant for the reaction of **13** to **14** (12). This catalyst system had an activity orders of magnitude higher than the previously most reactive Ru(II) (13) or Ce(IV) (14) complexes.

The synthesis of isoxazoles **16** from two terminal alkynes **15** and a $HNO_3/NaNO_2$ oxidation system with $Na[AuCl_4]$ was discovered by Natile *et al.* (15), Figure 10.

The latter reaction used the knowledge that alkynes are excellent substrates for gold catalysts. This had been recognised several years before by Utimoto *et al.*, see the next but one section.

The oxidative carbonylation of amines **17** to formamides **18** was achieved using $AuCl(PPh_3)$ as catalyst and oxygen as oxidant (16), Figure 11. This gold complex had been used three years earlier by Teles *et al.* for the addition of oxygen-nucleophiles to alkynes, see the next but one section.

Nevertheless, this result was not unique for gold since palladium(II) gave comparable results. At higher temperatures and pressure with the same catalyst-system carbamates **19** were obtained (17), Figure 12.

The soluble complexes $Na[AuCl_4]$ and $AuCl(PPh_3)$ were reported to efficiently catalyse the oxidation of alkanes such as cyclooctane by H_2O_2 in acetonitrile at 75°C with a TON of 520. But the reaction was not selective, cyclooctyl hydroperoxide, cyclooctanone and cyclooctanole were obtained (18).

Further oxidations using H_2O_2 or its derivative $(Me_3Si)_2O_2$ were reported by Sundermeyer *et al.* (19). They observed that 5 mol% of both gold(I) and gold(III) complexes are active catalysts for the *Baeyer-Villiger* oxidation of ketones **20** (20), Figure 13. While the gold complexes had the highest activity, silver(I) complexes were also active and there was also a slow uncatalysed background reaction.

There was a spectacular report from Shilov *et al.* (21). A gold-containing protein ("Au-protein"), isolated from the goldophilic bacteria *Micrococcus luteos*, oxidises methane to methanol.

C-C-Bond Formation

The first example of a C-C-bond forming reaction catalysed by gold was the asymmetric aldol condensation developed by Ito, Hayashi *et al.* in 1986 (22). The addition of an isocyano acetate **23** to an aldehyde **22** produces *trans*-**24** as the major and *cis*-**25** as the minor product in excellent *enantiomeric excess (ee)* in the presence of a cationic gold catalyst and a chiral diphosphanyl ferrocene ligand, Figure 14.

This reaction had the highest impact on organic chemistry to date, and already several summarising reviews have appeared on the reaction and its application in organic synthesis (23,24).

Historically it is quite interesting to note that this was the first example of a catalytic asymmetric aldol reaction (25).

Just as an example, the synthesis of D-*threo*-sphingosine **28**, a membrane component, is shown in Figure 15. Here the stereoselective transformation of the aldehyde **26** to the oxazoline **27** is a key step.

The method could also be applied to *N*-tosylated aldimines, to give derivatives of enantiomerically pure α,β-diamino carboxylates (26).

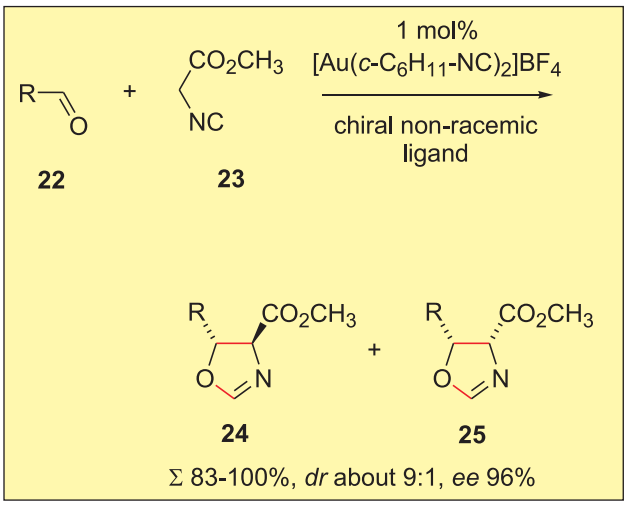

Figure 14
The very first example of a catalytic asymmetric aldol reaction (dr = diastereomeric ratio)

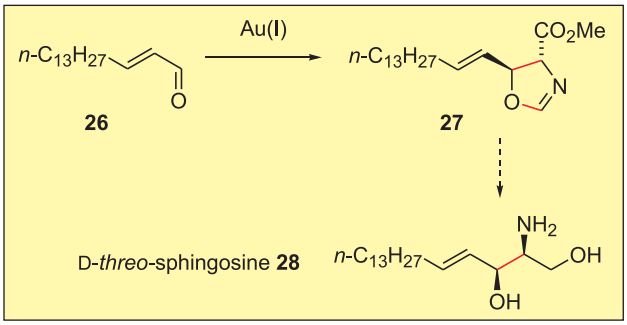

Figure 15
Key step in the synthesis of D-threo-sphingosine

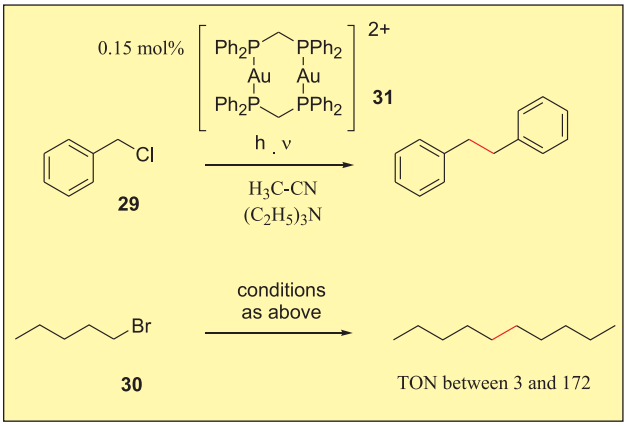

Figure 16
Photoinduced reductive dimerization

In 1992, Che *et al.* described a photoinduced C-C bond formation (27). As little as 0.15 mol% of the dinuclear complex **31** upon irradiation provided dimers of alkyl halides such as benzyl chloride **29** or pentyl bromide **30**, Figure 16. The turnover numbers varied from 3 to 172. The fate of the halogens is not discussed in detail, the triethylamine might

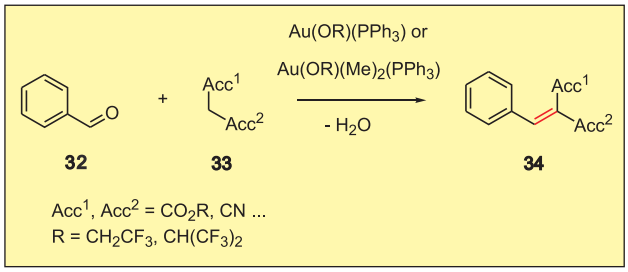

Figure 17
Knoevenagel condensations under neutral conditions

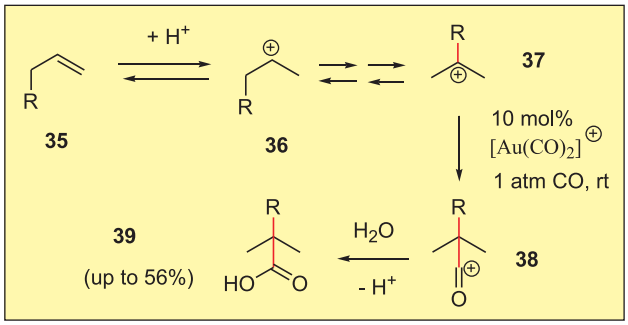

Figure 18
Koch-Haaf reactions at low CO pressure

be the reaction partner. The reaction probably proceeds via a radical mechanism.

Komiya *et al.* discovered that Au(I)- and Au(III)-alcoholates catalyse *Knoevenagel* condensations under neutral conditions (28). Acceptor-substituted methylene compounds **33** react with aldehydes **32** to provide alkenes **34**, Figure 17. This type of reaction where carbonyl groups react with nucleophiles, catalysed by gold, is encountered again in Figure 33 with substrate **88**.

Subsequently, Xu *et al.* reported that terminal olefins **35** with an Au(I)-catalyst, sulfuric acid (H_2SO_4) and only one atmosphere of carbon monoxide (CO) give tertiary carboxylic acids **39** (29), Figure 18. It is assumed that the H_2SO_4 first protonates the olefin and then the secondary carbenium ion **36** isomerises to a more stable tertiary carbenium ion **37** by so-called *Wagner-Meerwein* rearrangements (30,31,32); finally the carbon monoxide is transferred to this carbenium ion, the resulting acyl cation **38** is attacked by the nucleophile water and a proton is lost. Overall this transformation is a low-pressure equivalent of the *Koch-Haaf* reaction which normally needs up to 100 atm. of CO (33).

The transition-metal catalysed reactions of allenyl ketones such as **40** give different types of products **41**, **42** and **43** (34), Figure 19. With $AuCl_3$ the dimers **44** could be obtained as new products (35). It is also interesting to look at the reaction times; while the consumption of the starting material with 1 mol% of $AgNO_3$ took about one week and with 1 mol% of $PdCl_2(MeCN)_2$ about an hour, with 1 mol% $AuCl_3$ a complete conversion is achieved in less than 5

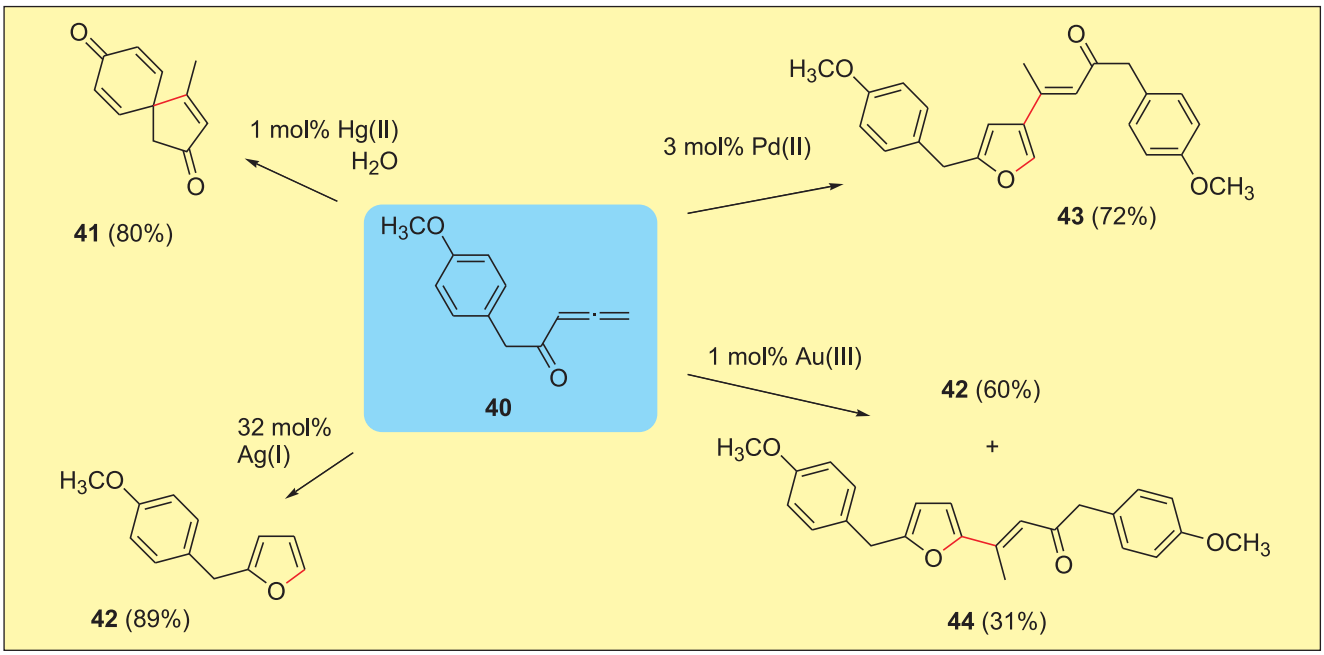

Figure 19
Allenyl ketones and different transition metal catalysts

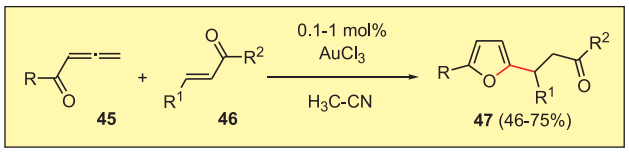

Figure 20
Selective cross-dimerization of allenyl ketones and Michael acceptors

minutes! Such faster kinetics produced by gold catalysts is not uncommon.

Furthermore, a cross-dimerization of allenyl ketones **45** and *Michael* acceptors (α,β-unsaturated ketones) **46** to substituted furans **47** could be achieved that way, a reaction that was impossible to achieve with the other late transition metal catalysts, Figure 20.

For the latter reaction, we could show that it is composed of two independent gold-catalysed parts, the isomerisation of the allenyl ketone **45** to a furan **48** and the reaction of **48** with the α,β-unsaturated ketone **46**, Figure 21. In the first part it is remarkable that unlike palladium(II), where the organometallic intermediate is long-lived and finds time to react with a second allenyl ketone, the gold undergoes a fast proto-demetallation. In the second part two different possibilities exist, which have a common intermediate **49**. This intermediate **49** is the gold-analogue of the intermediate of a well-known palladium-catalysed coupling reaction, the Heck reaction (36). In the Heck reaction this intermediate subsequently undergoes β-hydrogen elimination, but in the case of gold once again the proto-demetallation is faster and the saturated product **47** rather than the product **50** is set

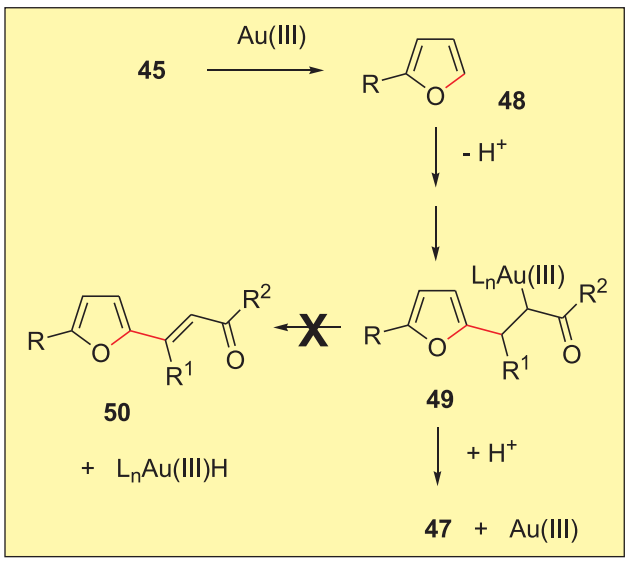

Figure 21
Proto-demetallation rather than β-hydride-elimination as characteristics of gold catalysts

free; the low tendency to form gold hydride complexes seems to be a general principle (37). Thus unlike palladium in the Heck reaction, gold does not undergo a change in oxidation state during the catalytic cycle.

Not only the heterocycle furan, but also a whole range of electron-rich benzenoid aromatic compounds can be used in such hydroarylation reactions of *Michael* acceptors catalysed by gold(III). Gold(I) showed lower turnover frequencies (38).

The activation of alkynes not only for the cycloisomerisation of a propargyl ketone to a furan but also

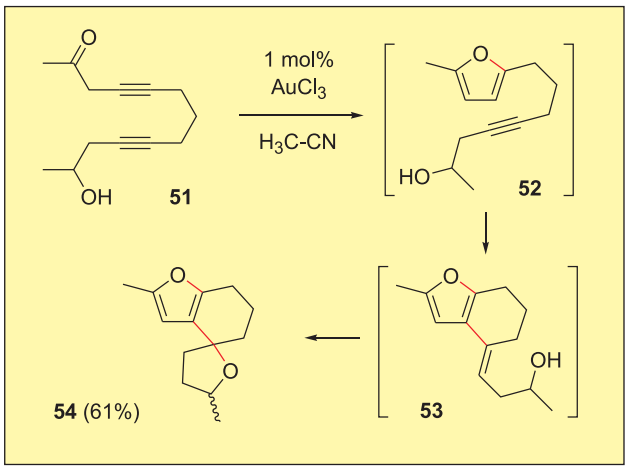

Figure 22
Cycloisomerisation, hydroarylation and nucleophilic cyclization in one step

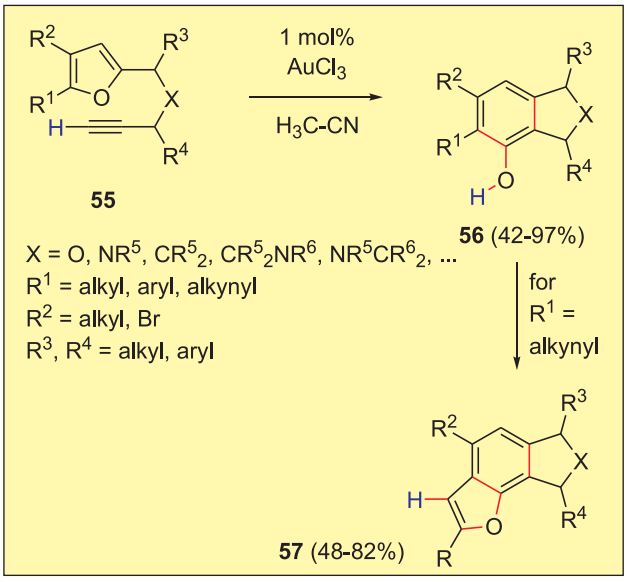

Figure 23
Synthesis of highly substituted phenols

for the intramolecular hydroarylation of an alkyne and, in the final step, even the intramolecular addition of an hydroxyl group to an alkene are part of the reaction of **51** to **54** via **52** and **53** (34), Figure 22.

The alkyne moiety is the functional group which has been most versatile in organic synthesis so far (39) as Figure 10 and numerous examples on the next pages show.

If, as in **55**, not a substituted but a terminal alkyne is tethered to the furan, the reaction takes an entirely different pathway. Highly substituted phenols **56** are generated (40), Figure 23. While other late transition metals with d^8-configuration are also capable of catalysing this reaction, gold is much more active than all the other catalysts. This reaction has been applied to the synthesis of biaryl

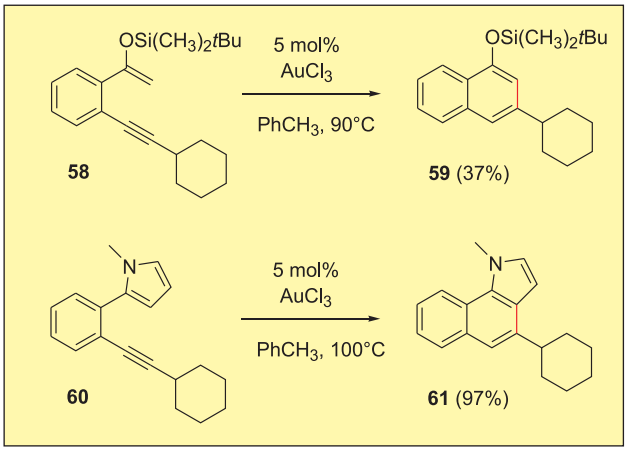

Figure 24
Further intramolecular vinylations of arenes

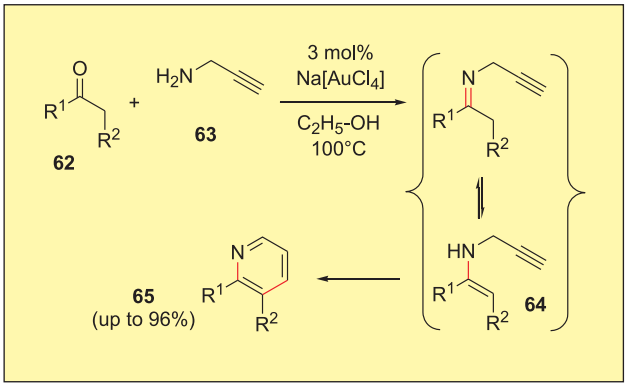

Figure 25
A new pyridine synthesis

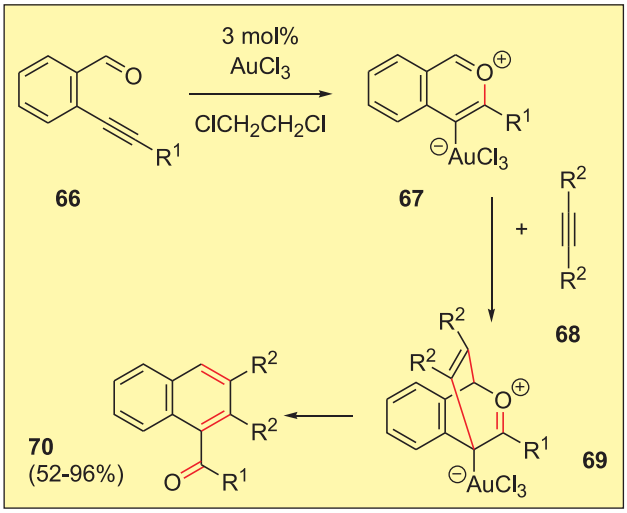

Figure 26
A new naphthalene synthesis

compounds (41), benzofurans **57** (42), recently in the total synthesis of *Jungianol* (43) and current work on the total synthesis of naturally occurring and pharmaceutically important tetrahydroisoquinolines (44,45).

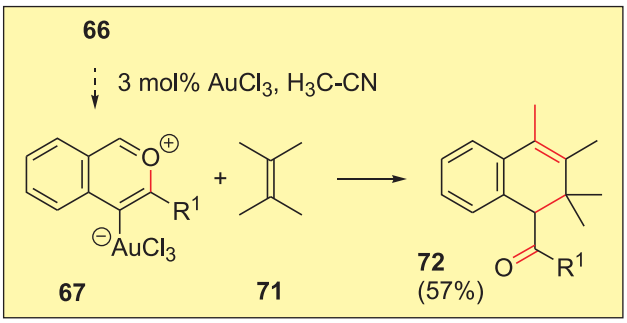

Figure 27
A dihydronapthalene synthesis

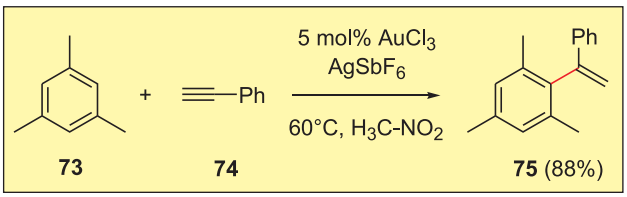

Figure 28
Intermolecular vinylation of arenes

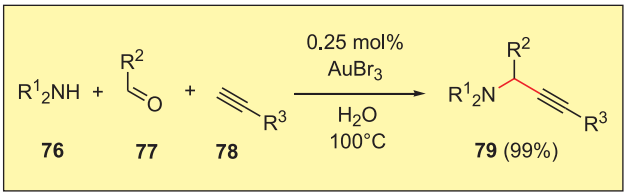

Figure 29
Synthesis of propargylamine, a three-component reaction in water

The principle mentioned above for **51**, the electrophilic attack of an activated alkyne (activated by co-ordination to gold) at an electron rich π-system such as an enol-ether **58** or a pyrrole **60** led to napthalene **59** or anellated napthalene systems **61** (46), Figure 24.

The analogous reaction leading to phenanthrenes was investigated by Fürstner *et al.* (47). Often $AuCl_3$ gave the highest yield and the highest chemoselectivity in comparison with $GaCl_3$, $InCl_3$ and $PtCl_2$.

A new synthesis of pyridines **65**, just published by Arcadi *et al.* (48), utilizes both the principle of the electrophilic attack of an alkyne at an electron-rich enamine in the intermediate **64** and in a preceding step the gold-catalysed condensation of ketones **62** with propargyl amines **63**, Figure 25 (compare formation of compound **92** in Figure 33).

Another synthesis of naphthalene systems similar to **59**, but by an entirely different route, was published by Yamamoto *et al.* in 2002 (49). From two different components, an *ortho*-alkynyl benzaldehyde **66** and a disubstituted alkyne **68**, 1-acylnapthalenes **70** are produced via **67** and **69**, Figure 26. Under similar conditions a copper(II) triflate/acid catalyst delivers only unsubstituted napthalenes (50).

Last year Dyker *et al.* proved that olefins such as **71** can also react with **67** to deliver products of type **72** (51), Figure 27.

Just recently, Reetz *et al.* discovered that the intermolecular variation of that reaction, terminal aryl alkynes **74** react with the electron-rich aromatic mesitylene **73** to **75** (52), Figure 28.

Three different components can be combined in a reaction developed by Li *et al.* in 2003 (53). From a secondary amine **76**, an aldehyde **77** and a terminal alkyne **78** the tertiary propargyl amine **79** is obtained in high yields in water as the solvent, Figure 29.

Li *et al.* were also the first to use $AuBr_3$ as the catalyst, which is in fact slightly cheaper per mol than $AuCl_3$. Yamamoto *et al.* (50) have already taken up this idea in their recent investigation of the naphthalene synthesis already cited above.

Furthermore, water was the optimal solvent for that reaction, which is most remarkable in the context of the addition of water to alkynes described below.

Activation of C-C-Multiple Bonds for the Addition of *N*- and *O*-Nucleophiles

The activation of C-C-multiple bonds for the addition of nucleophiles by late transition metal species such as Pd(II)

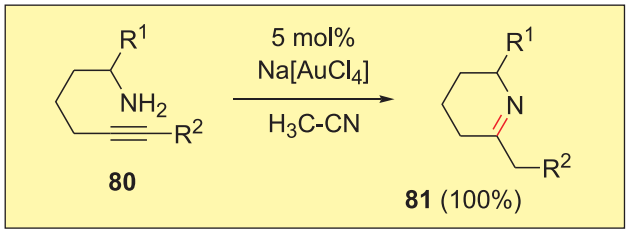

Figure 30
Intramolecular addition of N-nucleophiles to alkynes

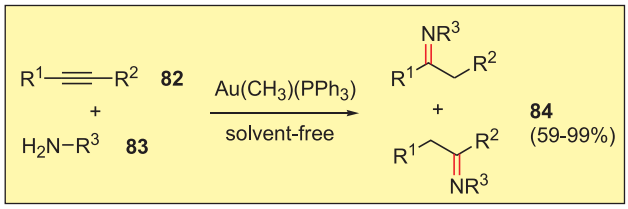

Figure 31
Hydroamination under solvent-free conditions

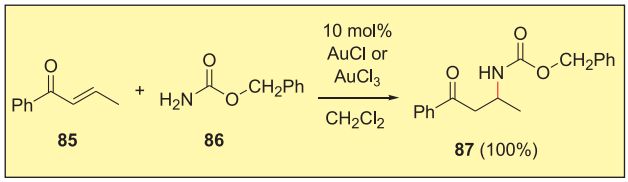

Figure 32
The aza-Michael reaction

is well known. Utimoto *et al*. published in 1987 that Au(III), which has the similar d^8-configuration, is much more efficient for the activation of alkynes **80** for the intramolecular addition of amines (54,55). Consequently nitrogen-heterocycles such as **81** can be obtained, Figure 30.

T. E. Müller *et al*. reported that a gold(III)-phosphane complex with a weakly co-ordinating nitrate counter ion was active for the hydroamination of alkynes, but a cationic copper(I)-catalyst possessed the highest activity (56,57).

Lok *et al*. also used a cationic gold(I) catalyst for the hydroamination to dihydropyrimidine-heterocycles, but $AgBF_4$ had the same activity (58).

Latest results of Tanaka *et al*. (59) showed that with the combination of $AuCH_3(Ph_3P)$ and an acidic promoter [a catalyst system developed by Teles *et al*. (69,70) for the addition of oxygen-nucleophiles to alkynes and allenes, see Figs 37 and 38], only 0.01 mol% of catalyst are needed and 86% yield of **84** could be obtained under solvent-free conditions from **82** and **83**, Figure 31.

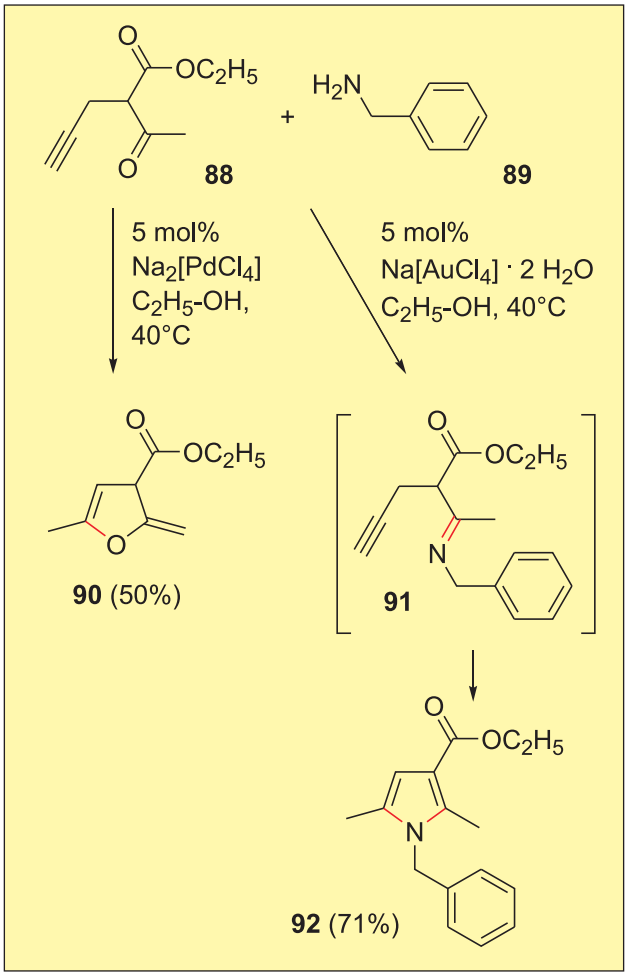

Figure 33
Different heterocycles from the same substrates by the choice of the catalyst

The addition of carbamates **86** to α,β-unsaturated ketones **85**, the *aza-Michael* reaction to **87**, could be achieved with 10 mol% of both AuCl and $AuCl_3$ (60), Figure 32.

A variation of the intramolecular addition of *N*-nucleophiles to alkynes was recently reported by Arcadi *et al*. (61). They observed that an amine **89** does not *intermolecularly* add to the alkyne in **88** but that $Na[AuCl_4] \cdot H_2O$ catalyses the condensation of the amine with a carbonyl group (62) and then the *intramolecular N*-nucleophile in **91** reacts with the alkyne and produces the pyrrole **92**, Figure 33. On the other hand, the corresponding Pd-catalyst $Na_2[PdCl_4]$ does not catalyse the condensation, and the intramolecular addition of the oxygen atom of the aldehyde group gives the oxygen-heterocycle **90**.

The same reaction was also conducted with primary amines possessing a stereogenic centre in the substituent (63). In continuation of this work, the gold-catalysed condensation of 1,3-dicarbonyl compounds **93** with

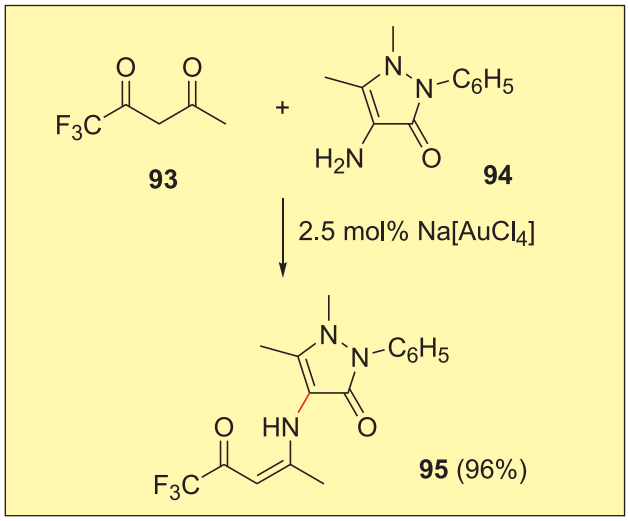

Figure 34
Selective condensation reactions to give enaminones

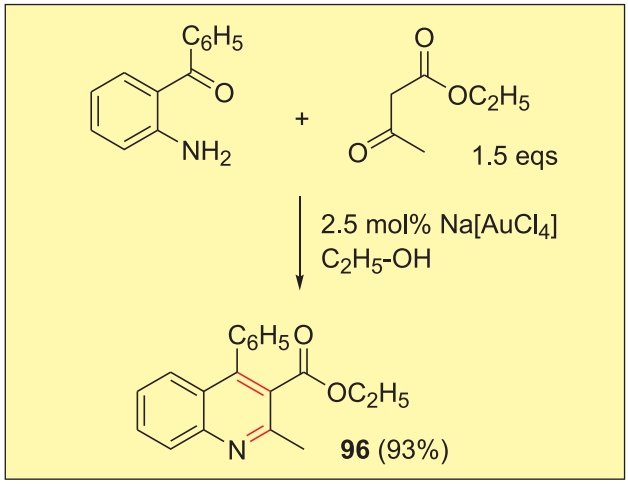

Figure 35
A new synthesis of quinolines

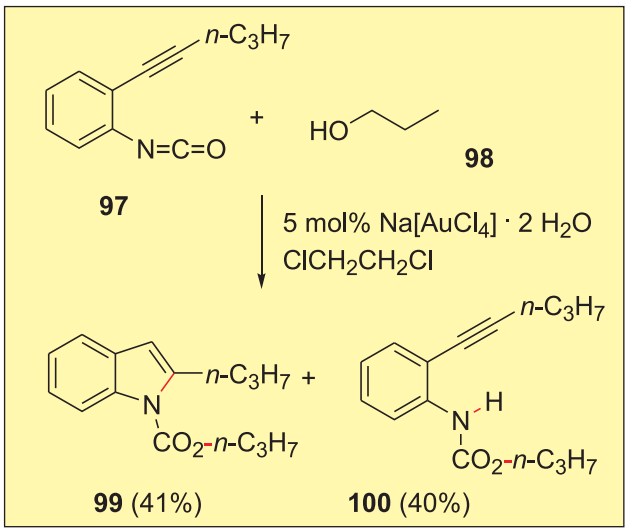

Figure 36
Indoles by gold catalysis

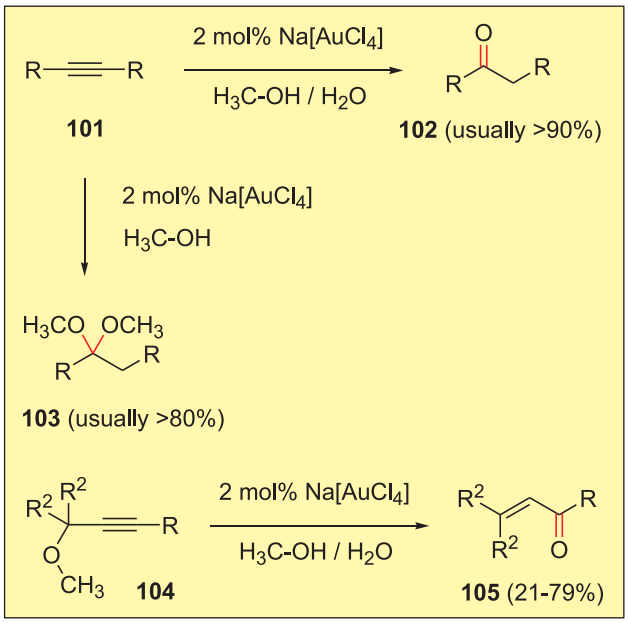

Figure 37
Intermolecular addition of O-nucleophiles to alkynes

nucleophiles was developed (62). Thus, with amines **94** β-enaminones **95** could be obtained under mild conditions in high yields, Figure 34.

Salts of other metals, such as CuI, $ZnCl_2$, $AgNO_3$ and $Na_2[PdCl_4]$ gave significantly lower yields. The reaction could be extended to alcohols, phosphanes and even thiols!

Subsequently, this was extended to an alternative protocol for the *Friedländer* synthesis of quinolines **96**, a substructure frequently found in pharmacologically active compounds (64), Figure 35. Here neither $Na_2[PdCl_4]$, CuI nor $AgNO_3$ showed catalytic activity, only $ZnCl_2$ gave some product.

Yamamoto *et al.* (65) reported that 2-alkynyl phenylisocyanates **97** and propanol **98** delivered a mixture of

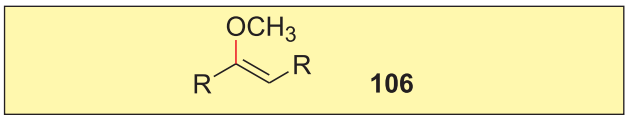

Figure 38
Enol ethers as side products in the addition of alcohols to alkynes

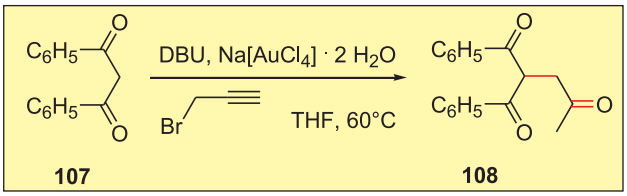

Figure 39
One-pot alkylation/hydration (DBU = 1,8-diazabicyclo[5.4.0]undec-7 -ene, THF = tetrahydrofuran)

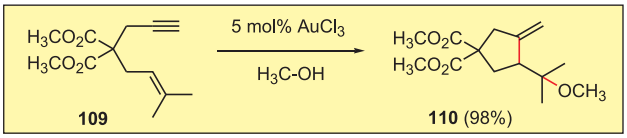

Figure 40
Inserting an olefin between the alkyne and the nucleophile

indole **99** (C-N-bond formation) and/or carbamate **100** (N-H-bond formation), Figure 36. Both $Na[AuCl_4] \cdot 2\ H_2O$ and $AuCl_3$ gave 80% of a mixture of **99** and **100** (ratio close to 1:1), while $Na_2[PdCl_4]$ gave a 74% yield of **99** and $Pd_2(dba)_3 \cdot CHCl_3$ provided 96% of **100**.

Similar additions to alkynes **101** could be achieved in an intermolecular manner with oxygen-nucleophiles such as water (to furnish ketones **102**) or alcohols (to furnish ketals **103**) (66,67). In unsymmetric alkynes the regioselectivity could be controlled by a neighbouring alkoxy group such as that in **104**, which finally gives α,β-unsaturated ketones **105** (68), Figure 37.

One major breakthrough in this field (and probably in the whole field of gold-catalysis, too) was the discovery published by Teles *et al.* in 1998. A cationic Au(I) catalyst with phosphane ligands provided ketals such as **103** along with the enol ether **106** from symmetrical alkynes with turnover numbers up to 100,000 and turnover frequencies up to 5,400/h (69,70), Figure 38.

These numbers were exceeded by Tanaka, Hayashi *et al.*, who succeeded in triplicating these turnover frequencies to 15,600 by the choice of methanol as the solvent and CO as a co-ligand for the addition of water to alkynes (71). Although the reaction is conducted in aqueous methanol, only the thermodynamically more stable addition product of water, i.e. the ketone, is produced. As expected, the *Markovnikov*-product is observed. The TON is orders of magnitude higher than the most efficient catalysts based on other metal derivatives such as *cis*-$PtCl_2[P(m\text{-}C_6H_4SO_3Na)_3]_2$ (72).

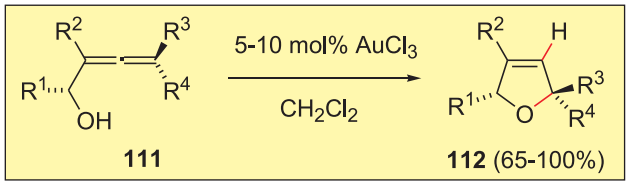

Figure 41
Clean axial to central chirality transfer with allenyl carbinols

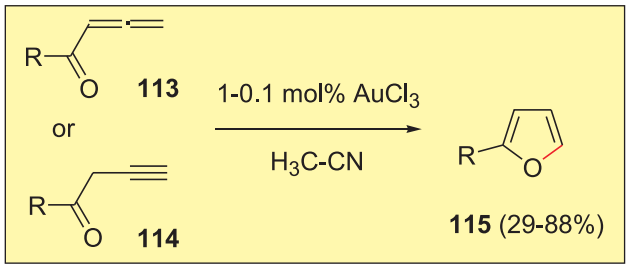

Figure 42
Ketones as intramolecular oxygen-nucleophiles

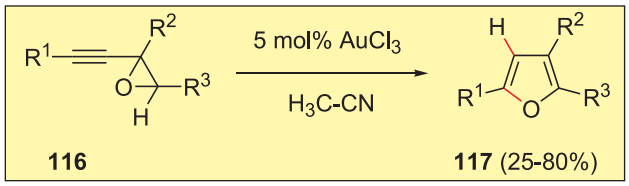

Figure 43
Epoxides as intramolecular oxygen-nucleophiles

Arcadi *et al.* (73) described the selective mono-propargylation of dibenzoylmethane **107** in the presence of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) followed by a $Na[AuCl_4] \cdot 2\ H_2O$-catalysed hydration to the tricarbonyl derivative **108** as a one-pot procedure, Figure 39.

Organometallic thiazolium gold(III)-complexes could also catalyse the hydration of phenylacetylene in ionic liquids (74). The optimum reaction temperature was 30°C, the 1-butyl-3-methylimidazolium triflate in combination with 2.4 mol% $Na[AuCl_4]$ delivered a yield of up to 75%.

Another example for such gold complexes of *N*-heterocyclic carbenes being active in the hydration of 3-hexyne was provided recently by Herrmann *et al.* (75).

Most interesting is recent research by M. Laguna *et al.* (76), who investigated organometallic gold(III) and gold(I) complexes for the addition of water and methanol to alkynes and obtained evidence for gold(III) being the active catalyst.

An olefin is used as a relay for the addition of alcohols to 1,6-enynes **109** catalysed by $AuCl_3$. Echavarren *et al.* (77) reported that, at least in some examples, the results obtained with $AuCl_3$ were superior to the results observed with $PtCl_2$ for the formation of **110**, Figure 40.

A different type of C-C-multiple bond is an allene such as **111**. The intramolecular addition of alcohol groups was described by Krause *et al.* (78). The axial chirality of the allene in **111** unit cleanly transfers to a central chirality in the dihydrofuran **112**, Figure 41. This was the method of choice for acid-sensitive substrates which would not survive classical acid-catalysed cyclization.

This reaction was also a key step in the preparation of an important intermediate of Marshall's citreovial synthesis (79). Rather than the almost stoichiometric amounts of $AgNO_3$ (80 mol%) used with silver, only 5 mol% $AuCl_3$ was necessary (80).

A related reaction of allenyl ketones **113** to furans **115** had already been reported in 2000 by Hashmi *et al.* (34); propargyl ketones **114** react in a similar manner, Figure 42.

A further type of oxygen-nucleophile are epoxides, the intramolecular reaction of alkynyl epoxides **116** readily produces furans **117** with a perfect control of the position of the substituents (81), Figure 43.

Reactions with Organoboron Compounds, Dihydrogen, Organostannanes and Organosilanes

Studies on these reactions were initiated in 1995 by Baker, Westcott *et al.* (82). This work also provided experimental proof for a principle of gold chemistry deduced much earlier

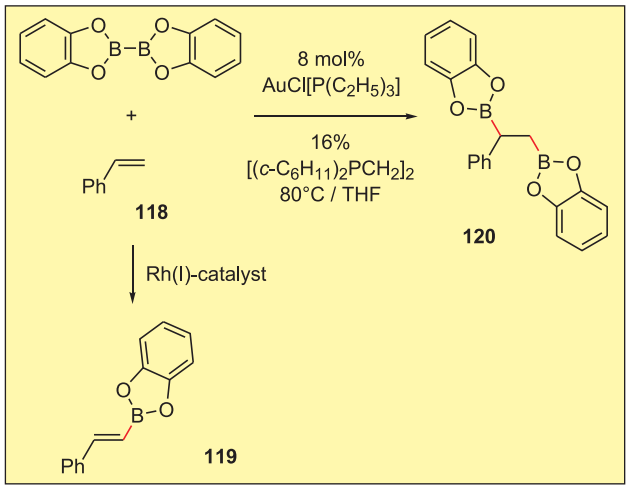

Figure 44
Diborylation of styrenes - no competing β-H-elimination (THF = tetrahydrofuran)

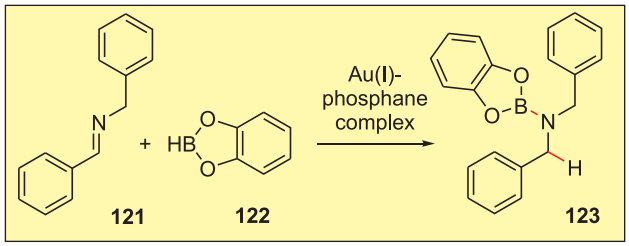

Figure 45
Intermolecular hydroboration of imines

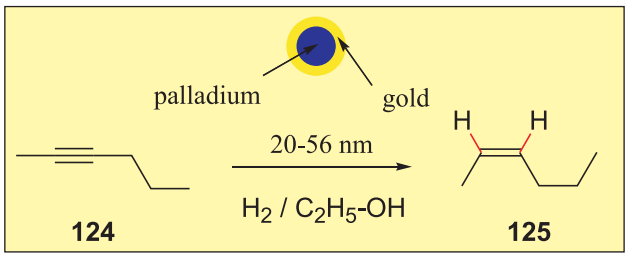

Figure 46
Hydrogenation of alkynes to (Z)-akenes

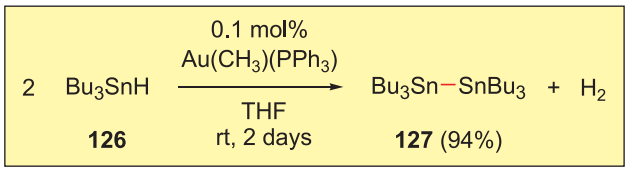

Figure 47
Dehydrogenative dimerisation of trialkylstannanes (THF = tetrahydrofuran)

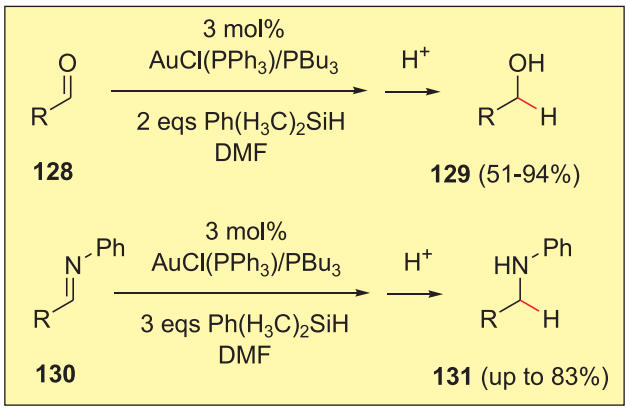

Figure 48
Hydrosilylation of aldehydes and imines (DMF = N,N-dimethylformamide)

from the lack of gold hydrides, i.e. the low tendency to undergo β-hydride elimination (compare Figure 21). The diborylation of styrenes **118** was unsuccessful with rhodium catalysts, only the vinyl boranes **119** were obtained. But, with the gold(I)-catalyst the diboryl compound **120** was isolated, Figure 44. Most unfortunately no yield is given, so that the turnover number cannot be calculated.

The hydroboration of arylimines **121** with **122** was also possible, the phosphane gold(I)-chloride complex catalysed reaction to give **123**, Figure 45: this was more than 40 times faster than the uncatalysed reaction (83).

The selective hydrogenation of alkynes such as **124** to (*Z*)-alkenes **125** is an important topic in organic synthesis. Here, Schmid *et al.* were quite successful with gold-covered palladium particles of 20-56 nm diameter (84). Up to a conversion of 80%, the selectivity is high for the (*Z*)-product and these catalysts are more active than the pure metals.

Hexaalkyldistannane is a useful reagent for organic synthesis (85), but it is relatively expensive. This immediately clarifies the importance of the formation of hexabutyldistannane **127** from the relatively inexpensive tributylstannane **126** by dehydrogenative dimerization forming the tin-tin-bond as described by Ito *et al.* in 1999 (86).

In 2000, Hosomi *et al.* reported the successful hydrosilylation of ketones **128** and imines **130** with $PhMe_2SiH$ and 3 mol% of the $AuCl(PPh)_3/PBu_3$ catalyst (87). After workup, the primary alcohols **129** or the secondary amines **131** could be isolated.

This methodology allows a differentiation between aldehydes and ketones.

Trans/cis-Isomerisation of Pd(II)-Diarylcomplexes

The *trans*/*cis*-isomerisation of square-planar d^8-complexes had been of interest in co-ordination and organometallic chemistry for a long time. In 1998 Espinet *et al.* discovered that as little as 0.6 mol% of an aryl gold(I)-tetrahydrothiophene complex catalyses the isomerisation of the *trans*-complex **132** to the *cis*-complex **133** within minutes, while the uncatalysed reaction under the same conditions would take days (88), Figure 49.

Curiosities

As early as 1990, Herrmann *et al.* filed an interesting patent, where numerous transition metal complexes, including three gold complexes, of tris(*m*-sulfonphenyl)phosphate were

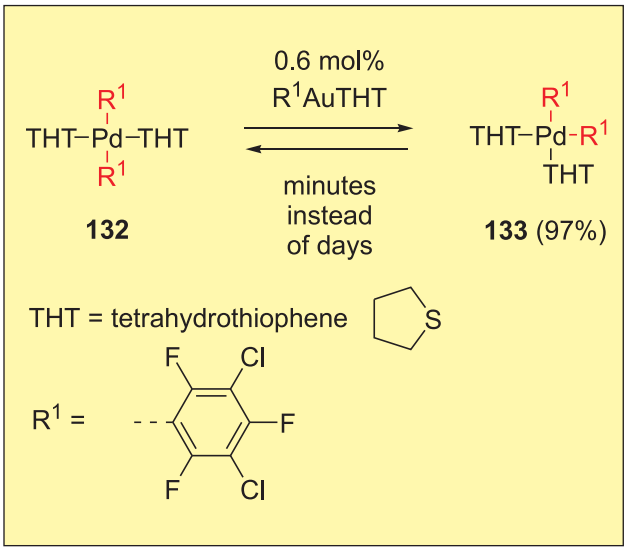

Figure 49
Acceleration of the trans/cis-isomerisation in Pd(II)-complexes

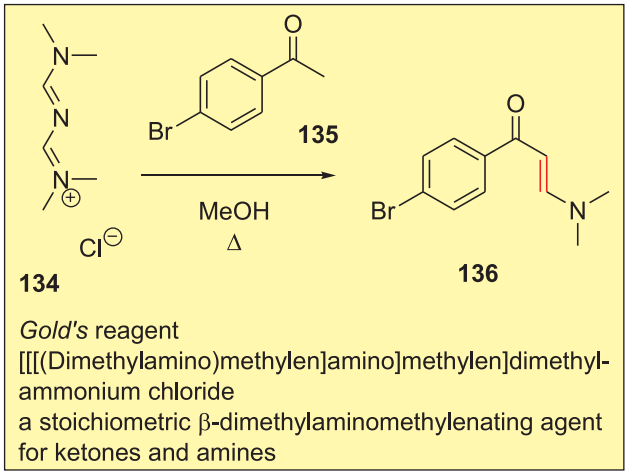

Figure 50
Gold's reagent does not contain any gold!

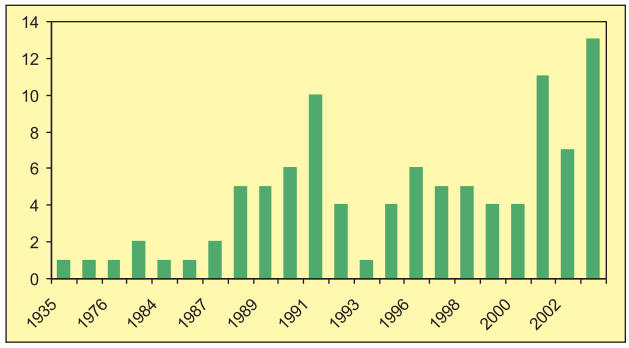

Figure 51
Publications on homogeneous catalysis per year

prepared (89,90,91). A use as catalysts in homogeneous hydrogenations, the water gas shift reaction, hydroformylations, oxidations, carbon-carbon cross-linking reactions and hydroamination was claimed, but none of the examples for catalysis reactions given in the patent was conducted with gold. With the many reactions known today, it would be quite interesting to look at these complexes again!

There exists a name-reagent, Gold's reagent **134**. Remarkably it does not contain the element gold; it is a stoichiometric β-dimethylaminomethylenating agent for ketones like **135** (to yield **136**) or amines (92,93), Figure 50.

Conclusions

It is obvious that homogeneous catalysis by gold already has numerous applications. Most of these are in the field of organic synthesis (of fine chemicals), and only the reactions in Figure 47 (stannanes) and in Figure 49 (Pd complexes) stem from the field of inorganic synthesis.

Overall, the following 'fundamentals' of homogeneous gold-catalysis can be deduced from the examples above:

1) Gold is a 'soft' transition metal and thus prefers other soft partners, for example carbon (this might explain the dominance of organic chemistry in this field).
2) Gold shows a low tendency for β-hydride elimination.
3) Gold often reacts much faster than other transition metals which in principle can catalyse the same reaction. Often this higher reactivity cannot only be explained by higher ligand exchange rates. Here theoretical investigation might provide some insight.
4) Organogold intermediates undergo fast proto-demetallation.
5) Due to the easy reduction and the difficult oxidation of gold, a cross-coupling chemistry seems to be difficult to reach due to the necessary change of oxidation states and most reactions presented here probably do not go along with oxidation or reduction of the catalytically active gold species in the catalytic cycle (94,95,96,97).
6) In most cases, the mechanism of the reactions, starting with the oxidation state of the catalytically active species, has not yet been established. It is also obvious that often the reactions are possible with both Au(I) or Au(III) pre-catalysts and the question of what is the oxidation state of the active species has also not yet been resolved.

Most of the different homogeneous reactions catalysed by gold have been developed in the past four years. The distribution of the papers on homogeneous gold catalysis in time is shown in Figure 51.

One can clearly see two major 'peaks', one was probably initiated in 1986 by Ito and Hayashi's discovery of the asymmetric aldol reaction, the second can be related to both Teles' (69,70) 1998 finding of highly active catalysts for the addition of heteronucleophiles to alkynes and the Dyker (98) 'Highlight' paper from 2000 on the C-C-bond formation reactions developed by Hashmi *et al.* in 2000 (34,40).

I am confident, that these developments will accelerate in the near future, and that most people working in the field of homogeneous transition metal catalysis will also give gold a chance on a regular basis.

Acknowledgements

My co-workers Lothar Schwarz, Tanja M. Frost, Li Grundl (Li Ding), Elzen Kurpejovic, Jan Weyrauch, Dirk Fischer, Pradipta Sinha, Ralph Salathé and Matthias Rudolph have added major contributions to the field, many aspects not being cited in this paper. I am also grateful to our sponsors DFG, Fonds der Chemischen Industrie, DAAD, Karl-Ziegler Stiftung and Umicore AG & Co KG (formerly OMG, dmc^2, Degussa).

About the Author

A. Stephen K. Hashmi is professor of organic chemistry at the Universität Stuttgart. He carried out his Diploma and PhD with Professor G. Szeimies at the Ludwig-Maximilians-Universität München in the field of strained organic compounds such as bicyclobutanes and propellanes. His postdoctorate research with Professor B. M. Trost at Stanford University, California, covered transition metal catalysis, specifically then enyne metathesis. His Habilitation with Prof. J. Mulzer at the Freie Universität Berlin, the Johann Wolfgang Goethe-Universität Frankfurt and the Universität Wien, Austria, as well as visits at the University of Tasmania, Australia, and the Universität Marburg focused on both stoichiometric organometallic chemistry and transition metal catalysed organic reactions, which are still the major topics in the group. Recently, activities in the field of bioorganometallic chemistry with enantiomerically pure metallacycloalkanes have been added.

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